

Appl. No. 10/666,192

Amdt. dated June 15, 2006

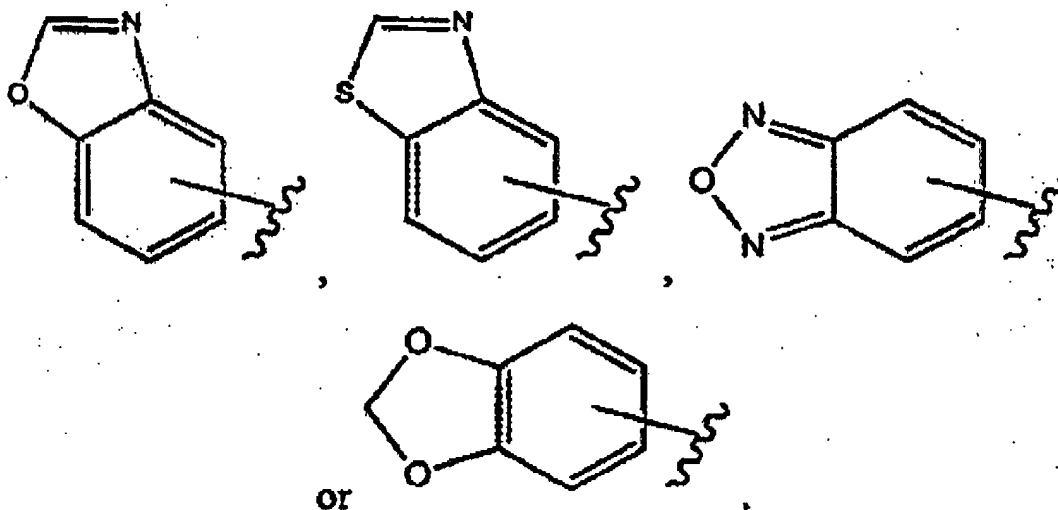
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Amendments to the claims

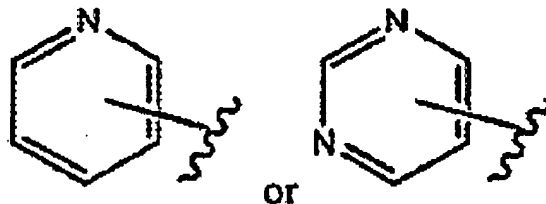
This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims

1. (cancelled)
2. (cancelled)
3. (withdrawn) A compound of claim 1, wherein R¹ is



4. (withdrawn) A compound of claim 1, wherein R¹ is

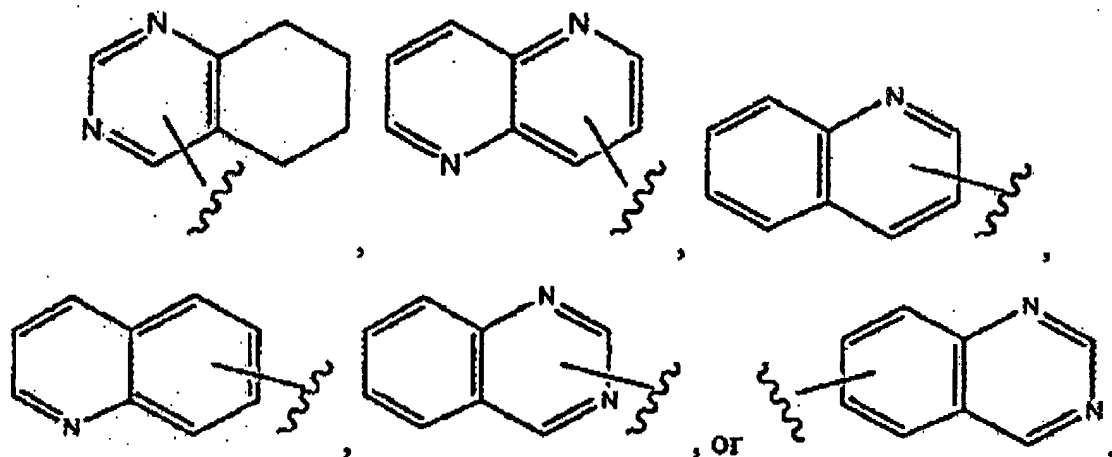


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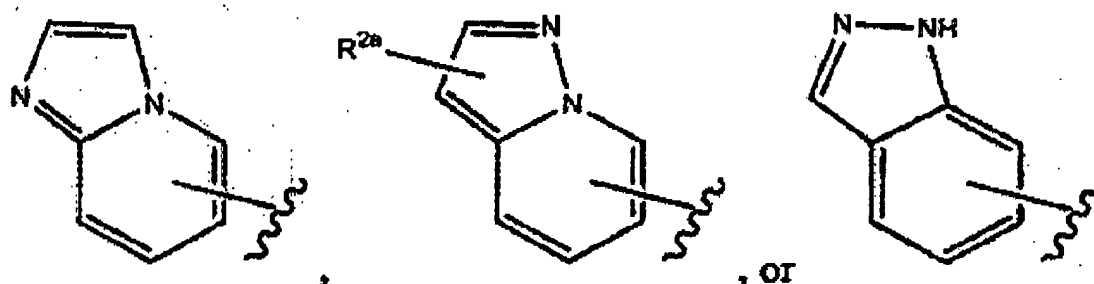
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5. (withdrawn) A compound of claim 1, wherein R^1 is



6. (withdrawn) A compound of claim 1, wherein R^1 is

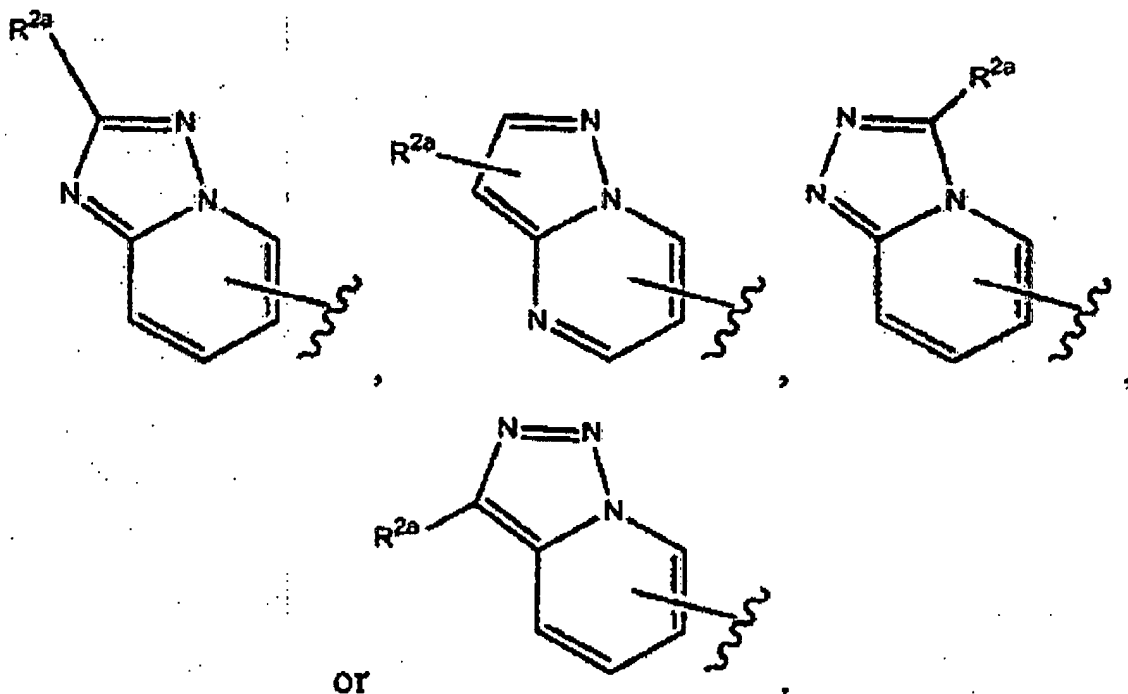


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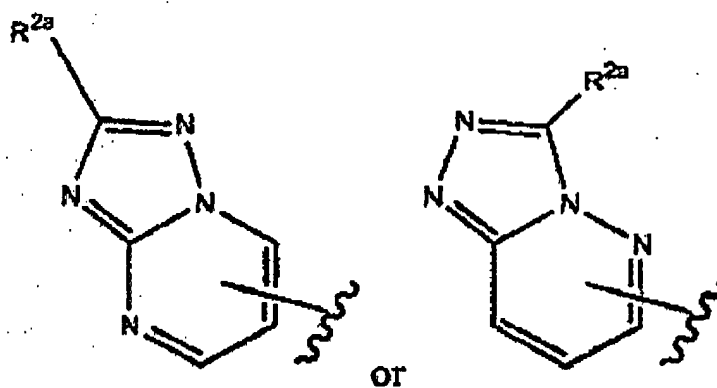
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7. (withdrawn) A compound of claim 1, wherein R^1 is



8. (withdrawn) A compound of claim 1, wherein R^1 is



9. (currently amended) A compound of claim 14, wherein s is one to two; R^3 is hydrogen or (C_1-C_6) alkyl; R^4 is hydrogen, (C_1-C_6) alkyl, perhalo (C_1-C_6) alkyl, phenyl, (C_1-C_6) alkyl-S- $(C_1-$

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C₆alkyl-, (C₃-C₁₀)heteroaryl, (C₃-C₁₀)cycloalkyl, aminoalkyl, amino(C=O)-, (C₁-C₆alkyl-(C=O)-NH-(C₁-C₆alkyl, or (C₁-C₆alkyl-NH-(C=O)-(C₁-C₆alkyl; and R⁶ is H, (C₁-C₆alkyl, (C₃-C₁₀)cycloalkyl, (C₁-C₆alkyl-(SO₂)-(C₁-C₆alkyl, (C₁-C₆alkyl-(SO₂)-NH-(C₁-C₆alkyl, (C₁-C₆alkyl-NH-(SO₂)-(C₁-C₆alkyl, (C₁-C₆alkyl-(C=O)-(C₁-C₆alkyl, (C₃-C₁₀)cycloalkyl-(C=O)-(C₃-C₁₀)cycloalkyl, (C₁-C₆alkyl-NH-(C=O)-(C₁-C₆alkyl, (C₁-C₆alkyl-(C=O)-NH-(C₁-C₆alkyl, (C₃-C₁₀)cycloalkyl-NH-(C=O)-(C₃-C₁₀)cycloalkyl, or (C₃-C₁₀)cycloalkyl-(C=O)-NH-(C₃-C₁₀)cycloalkyl.

10. (original) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

11. (withdrawn) A method of preventing or treating a TGF-related disease state in an animal or human comprising the step of administering a therapeutically effective amount of a compound of claim 1 to the animal or human suffering from the TGF-related disease state.

12. (withdrawn) A method of claim 11, wherein said TGF-related disease state is selected from the group consisting of cancer, glomerulonephritis, diabetic nephropathy, hepatic fibrosis, pulmonary fibrosis, intimal hyperplasia and restenosis, scleroderma, and dermal scarring.

13. (new) A compound selected from the group consisting of:

1-Methyl-6-[5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-1H-benzotriazole;

6-[5-(6-Methyl-pyridin-2-yl)-1H-imidazol-4-yl]-1H-benzotriazole;

2-Methyl-5-[5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-2H-benzotriazole;

2-Methyl-5-[2-methyl-5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-2H-benzotriazole;

6-[2-tert-Butyl-5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-1H-benzotriazole;

1-Methyl-6-[5-(6-methyl-pyridin-2-yl)-2-tifluoromethyl-1H-imidazol-4-yl]-1H-benzotriazole;

6-[2-Methyl-5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-1H-benzotriazole;

1-Methyl-6-[2-methyl-5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-1H-benzotriazole;

1-Methyl-6-(2-methyl-5-pyridin-2-yl-1H-imidazol-4-yl)-1H-benzotriazole;

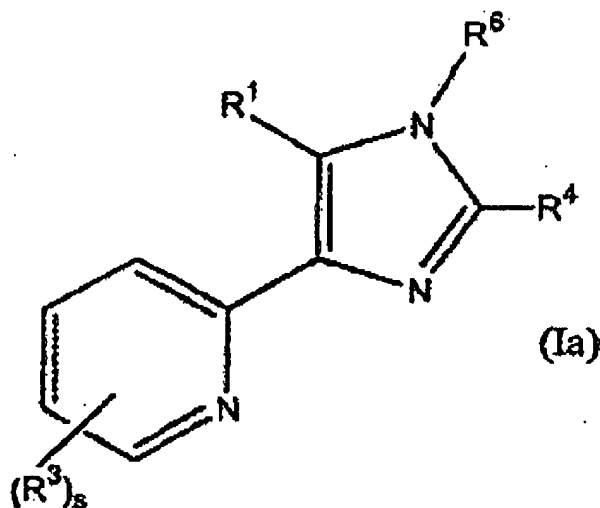
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1-Methyl-6-[5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-1H-benzotriazole;
5-[2-(2-Benzo[1,3]dioxol-5-yl-1-methyl-ethyl)-5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-2-methyl-2H-benzotriazole;
2-Methyl-5-[5-(6-methyl-pyridin-2-yl)-2-(2-methylsulfanyl-ethyl)-1H-imidazol-4-yl]-2H-benzotriazole;
2-Methyl-5-[5-(6-methyl-pyridin-2-yl)-2-thiazol-2-yl-1H-imidazol-4-yl]-2H-benzotriazole;
6-[2-Cyclopropyl-5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-1-methyl-1H-benzotriazole;
5-[2-Cyclopropyl-5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-2-methyl-2H-benzotriazole;
6-[2-Cyclopropyl-5-(6-methyl-pyridin-2-yl)-1H-imidazol-4-yl]-quinoxaline;
[4-(2-Methyl-2H-benzotriazol-5-yl)-5-(6-methyl-pyridin-2-yl)-1H-imidazol-2-yl]-methanol; and
4-(2-Methyl-2H-benzotriazol-5-yl)-5-(6-methyl-pyridin-2-yl)-1H-imidazole-2-carboxylic acid amide.

14. (new) A compound of formula (Ia):



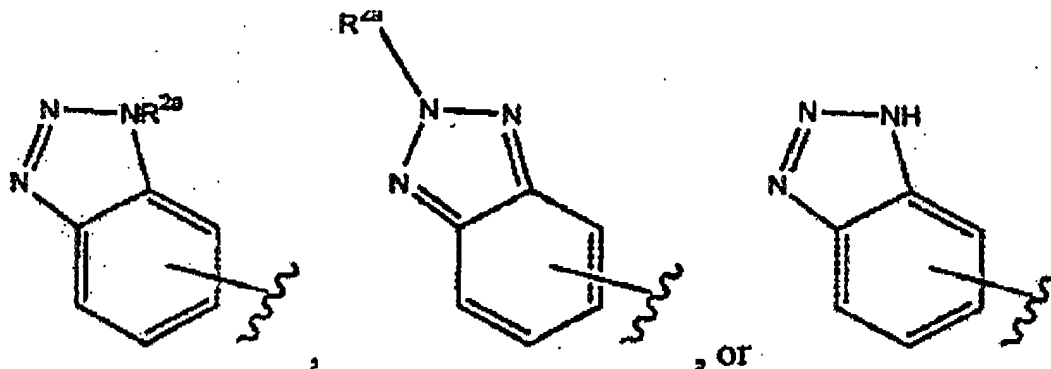
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or a pharmaceutically acceptable salt, prodrug, tautomer, hydrate, or solvate thereof, wherein:

R^1 is a benzotriazole selected from



wherein said benzotriazole can optionally be further independently substituted with at least one moiety independently selected from the group consisting of: carbonyl, halo, halo(C_1 - C_6)alkyl, perhalo(C_1 - C_6)alkyl, perhalo(C_1 - C_6)alkoxy, (C_1 - C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, hydroxy, oxo, mercapto, (C_1 - C_6)alkylthio, (C_1 - C_6)alkoxy, (C_5 - C_{10})aryl, (C_5 - C_{10})heteroaryl, (C_5 - C_{10})aryloxy, (C_5 - C_{10})heteroaryloxy, (C_5 - C_{10})ar(C_1 - C_6)alkyl, (C_5 - C_{10})heterar(C_1 - C_6)alkyl, (C_5 - C_{10})ar(C_1 - C_6)alkoxy, (C_5 - C_{10})heteroar(C_1 - C_6)alkoxy, HO-(C=O)-, ester, amido, ether, amino, amino(C_1 - C_6)alkyl, (C_1 - C_6)alkylamino(C_1 - C_6)alkyl, di(C_1 - C_6)alkylamino(C_1 - C_6)alkyl, (C_5 - C_{10})heterocyclyl(C_1 - C_6)alkyl, (C_1 - C_6)alkyl- and di(C_1 - C_6)alkylamino, cyano, nitro, carbamoyl, (C_1 - C_6)alkylcarbonyl, (C_1 - C_6)alkoxycarbonyl, (C_1 - C_6)alkylaminocarbonyl, di(C_1 - C_6)alkylaminocarbonyl, (C_5 - C_{10})arylcarbonyl, (C_5 - C_{10})aryloxycarbonyl, (C_1 - C_6)alkylsulfonyl, and (C_5 - C_{10})arylsulfonyl;

wherein R^{2a} is selected from the group consisting of carbonyl and carboxyl, or

R^{2a} is selected from the group consisting of (C_1 - C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, (C_3 - C_{10})cycloalkyl, (C_5 - C_{10})aryl, (C_1 - C_6)alkylaryl, amino, (C_2 - C_6)acid, (C_1 - C_6)ester, (C_5 - C_{10})heteroaryl, (C_5 - C_{10})heterocyclyl, (C_1 - C_6)alkoxy, nitro, halo, hydroxyl, (C_1 - C_6)alkoxy(C_1 - C_6)ester; each of which may be optionally substituted by at least one moiety independently selected from the group consisting of halo, (C_1 - C_6)alkyl, (C_2 - C_6)alkenyl, (C_2 - C_6)alkynyl, perhalo(C_1 - C_6)alkyl, phenyl, (C_3 - C_{10})cycloalkyl, (C_5 - C_{10})heteroaryl, (C_5 - C_{10})heterocyclic, formyl, NC-, (C_1 - C_6)alkyl-(C=O)-, phenyl-(C=O)-, HO-(C=O)-, (C_1 - C_6)alkyl-O-(C=O)-, (C_1 - C_6)alkyl-NH-(C=O)-, ((C_1 - C_6)alkyl)₂-N-(C=O)-, phenyl-NH-(C=O)-, phenyl-[(C_1 - C_6)alkyl]-N]-

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(C=O)-, O₂N-, amino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂-amino, (C₁-C₆)alkyl-(C=O)-NH-, (C₁-C₆)alkyl-(C=O)-[((C₁-C₆)alkyl)-N]-, phenyl-(C=O)-NH-, phenyl-(C=O)-[((C₁-C₆)alkyl)-N]-, H₂N-(C=O)-NH-, (C₁-C₆)alkyl-HN-(C=O)-NH-, ((C₁-C₆)alkyl)₂N-(C=O)-NH-, (C₁-C₆)alkyl-HN-(C=O)-[((C₁-C₆)alkyl)-N]-, ((C₁-C₆)alkyl)₂N-(C=O)-[((C₁-C₆)alkyl)-N]-, phenyl-HN-(C=O)-NH-, (phenyl)₂N-(C=O)-NH-, phenyl-HN-(C=O)-[((C₁-C₆)alkyl)-N]-, (phenyl)₂N-(C=O)-[((C₁-C₆)alkyl)-N]-, (C₁-C₆)alkyl-O-(C=O)-NH-, (C₁-C₆)alkyl-O-(C=O)-[((C₁-C₆)alkyl)-N]-, phenyl-O-(C=O)-NH-, phenyl-O-(C=O)-[((C₁-C₆)alkyl)-N]-, (C₁-C₆)alkyl-SO₂NH-, phenyl-SO₂NH-, (C₁-C₆)alkyl-SO₂-, phenyl-SO₂-, hydroxy, (C₁-C₆)alkoxy, perhalo(C₁-C₆)alkoxy, phenoxy, (C₁-C₆)alkyl-(C=O)-O-, (C₁-C₆)ester-(C₁-C₆)alkyl-O-, phenyl-(C=O)-O-, H₂N-(C=O)-O-, (C₁-C₆)alkyl-HN-(C=O)-O-, ((C₁-C₆)alkyl)₂N-(C=O)-O-, phenyl-HN-(C=O)-O-, and (phenyl)₂N-(C=O)-O-;

each R³ is independently selected from the group consisting of hydrogen and halo, or

R³ is independently selected from the group consisting of halo(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, perhalo(C₁-C₆)alkyl, phenyl, (C₅-C₁₀)heteroaryl, (C₅-C₁₀)heterocyclic, (C₃-C₁₀)cycloalkyl, hydroxy, (C₁-C₆)alkoxy, perhalo(C₁-C₆)alkoxy, phenoxy, (C₅-C₁₀)heteroaryl-O-, (C₅-C₁₀)heterocyclic-O-, (C₃-C₁₀)cycloalkyl-O-, (C₁-C₆)alkyl-S-, (C₁-C₆)alkyl-SO₂-, (C₁-C₆)alkyl-NH-SO₂-, O₂N-, NC-, amino, Ph(CH₂)₁₋₆HN-, (C₁-C₆)alkyl HN-, (C₁-C₆)alkylamino, [(C₁-C₆)alkyl]₂-amino, (C₁-C₆)alkyl-SO₂-NH-, amino(C=O)-, aminoO₂S-, (C₁-C₆)alkyl-(C=O)-NH-, (C₁-C₆)alkyl-(C=O)-[((C₁-C₆)alkyl)-N]-, phenyl-(C=O)-NH-, phenyl-(C=O)-[((C₁-C₆)alkyl)-N]-, (C₁-C₆)alkyl-(C=O)-, phenyl-(C=O)-, (C₅-C₁₀)heteroaryl-(C=O)-, (C₅-C₁₀)heterocyclic-(C=O)-, (C₃-C₁₀)cycloalkyl-(C=O)-, HO-(C=O)-, (C₁-C₆)alkyl-O-(C=O)-, H₂N(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-, [(C₁-C₆)alkyl]₂-N-(C=O)-, phenyl-NH-(C=O)-, phenyl-[(C₁-C₆)alkyl)-N]-(C=O)-, (C₅-C₁₀)heteroaryl-NH-(C=O)-, (C₅-C₁₀)heterocyclic-NH-(C=O)-, (C₃-C₁₀)cycloalkyl-NH-(C=O)- and (C₁-C₆)alkyl-(C=O)-O-; each of which may be optionally substituted by at least one substituent independently selected from the group consisting of (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, halo, H₂N-, Ph(CH₂)₁₋₆HN-, and (C₁-C₆)alkylHN-;

s is an integer from one to five;

R⁴ is independently selected from the group consisting of halo, or

R⁴ is independently selected from the group consisting of halo(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, perhalo(C₁-C₆)alkyl, phenyl, (C₅-C₁₀)heteroaryl, (C₅-

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(C₁₀)heterocyclic, (C₃-C₁₀)cycloalkyl, hydroxy, (C₁-C₆)alkoxy, perhalo(C₁-C₆)alkoxy, phenoxy, (C₅-C₁₀)heteroaryl-O-, (C₅-C₁₀)heterocyclic-O-, (C₃-C₁₀)cycloalkyl-O-, (C₁-C₆)alkyl-S-, (C₁-C₆)alkyl-S-(C₁-C₆)alkyl-, (C₁-C₆)alkyl-SO₂-, (C₁-C₆)alkyl-NH-SO₂-, O₂N-, NC-, amino, aminoalkyl, Ph(CH₂)₁₋₆HN-, (C₁-C₆)alkylHN-, (C₁-C₆)alkylamino, [(C₁-C₆)alkyl]₂-amino, (C₁-C₆)alkyl-SO₂-NH-, amino(C=O)-, aminoO₂S-, (C₁-C₆)alkyl-(C=O)-NH-, (C₁-C₆)alkyl-(C=O)-((C₁-C₆)alkyl)-N-, phenyl-(C=O)-NH-, phenyl-(C=O)-[((C₁-C₆)alkyl)-N]-, (C₁-C₆)alkyl-(C=O)-, phenyl-(C=O)-, (C₅-C₁₀)heteroaryl-(C=O)-, (C₅-C₁₀)heterocyclic-(C=O)-, (C₃-C₁₀)cycloalkyl-(C=O)-, HO-(C=O)-, (C₁-C₆)alkyl-O-(C=O)-, H₂N(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-, ((C₁-C₆)alkyl)₂-N-(C=O)-, phenyl-NH-(C=O)-, phenyl-[(C₁-C₆)alkyl)-N]-(C=O)-, (C₅-C₁₀)heteroaryl-NH-(C=O)-, (C₅-C₁₀)heterocyclic-NH-(C=O)-, (C₃-C₁₀)cycloalkyl-NH-(C=O)-, (C₁-C₆)alkyl-(C=O)-O-, (C₁-C₆)alkyl-(C=O)-NH-(C₁-C₆)alkyl, (C₁-C₆)alkyl-NH-(C=O)-(C₁-C₆)alkyl, and (C₁-C₆)alkyl-(C=O)-(C₁-C₆)alkyl, each of which may be optionally substituted by at least one moiety independently selected from the group consisting of (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo(C₁-C₆)alkyl, halo, H₂N-, NC-, HO-, Ph(CH₂)₁₋₆HN-, (C₁-C₆)alkylHN-, (C₅-C₁₀)heteroaryl and (C₅-C₁₀)heterocyclyl;

R⁶ is selected from the group consisting of (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, phenyl, (C₅-C₁₀)heteroaryl, (C₅-C₁₀)heterocyclic, (C₃-C₁₀)cycloalkyl, (C₁-C₆)alkyl-(SO₂)-, (C₁-C₆)alkyl-(SO₂)-(C₁-C₆)alkyl, phenyl-(SO₂), H₂N-(SO₂)-, (C₁-C₆)alkyl-NH-(SO₂)-, (C₁-C₆)alkyl-(SO₂)-NH-(C₁-C₆)alkyl, (C₁-C₆)alkyl-NH-(SO₂)-(C₁-C₆)alkyl, ((C₁-C₆)alkyl)₂N-(SO₂)-, phenyl-NH-(SO₂)-, (phenyl)₂N-(SO₂)-, (C₁-C₆)alkyl-(C=O)-, (C₁-C₆)alkyl-(C=O)-(C₁-C₆)alkyl, phenyl-(C=O)-, (C₅-C₁₀)heteroaryl-(C=O)-, (C₅-C₁₀)heterocyclic-(C=O)-, (C₃-C₁₀)cycloalkyl-(C=O)-, (C₃-C₁₀)cycloalkyl-(C=O)-(C₃-C₁₀)cycloalkyl, (C₁-C₆)alkyl-O-(C=O)-, (C₅-C₁₀)heterocyclic-O-(C=O)-, (C₃-C₁₀)cycloalkyl-O-(C=O)-, H₂N-(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-(C₁-C₆)alkyl, (C₁-C₆)alkyl-(C=O)-NH-(C₁-C₆)alkyl, phenyl-NH-(C=O)-, (C₅-C₁₀)heteroaryl-NH-(C=O)-, (C₅-C₁₀)heterocyclic-NH-(C=O)-, (C₃-C₁₀)cycloalkyl-NH-(C=O)-, (C₃-C₁₀)cycloalkyl-NH-(C=O)-(C₃-C₁₀)cycloalkyl, (C₃-C₁₀)cycloalkyl-(C=O)-NH-(C₃-C₁₀)cycloalkyl, ((C₁-C₆)alkyl)₂N-(C=O)-, (phenyl)₂N-(C=O)-, phenyl-[(C₁-C₆)alkyl)-N]-(C=O)-, (C₅-C₁₀)heteroaryl-[(C₁-C₆)alkyl)-N]-(C=O)-, (C₅-C₁₀)heterocyclic-[(C₁-C₆)alkyl)-N]-(C=O)-, and (C₃-C₁₀)cycloalkyl-[(C₁-C₆)alkyl)-N]-(C=O)-, each of which may be optionally substituted by at least one moiety independently selected from the group consisting of halo, (C₁-C₆)alkyl,

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(C₂-C₆)alkenyl, (C₂-C₆)alkynyl, perhalo(C₁-C₆)alkyl, (C₃-C₁₀)cycloalkyl, phenyl, benzyl, (C₅-C₁₀)heterocyclic, (C₅-C₁₀)heteroaryl, (C₁-C₆)alkyl-SO₂-, formyl, NC-, (C₁-C₆)alkyl-(C=O)-, (C₃-C₁₀)cycloalkyl-(C=O)-, phenyl-(C=O)-, (C₅-C₁₀)heterocyclic-(C=O)-, (C₅-C₁₀)heteroaryl-(C=O)-, HO-(C=O)-, (C₁-C₆)alkyl-O-(C=O)-, (C₃-C₁₀)cycloalkyl-O-(C=O)-, (C₅-C₁₀)heterocyclic-O-(C=O)-, (C₁-C₆)alkyl-NH-(C=O)-, (C₃-C₁₀)cycloalkyl-NH-(C=O)-, phenyl-NH-(C=O)-, (C₅-C₁₀)heterocyclic-NH-(C=O)-, (C₅-C₁₀)heteroaryl-NH-(C=O)-, ((C₁-C₆)alkyl)₂-N-(C=O)-, phenyl-(((C₁-C₆)alkyl)-N)-(C=O)-, hydroxy, (C₁-C₆)alkoxy, perhalo(C₁-C₆)alkoxy, (C₃-C₁₀)cycloalkyl-O-, phenoxy, (C₅-C₁₀)heterocyclic-O-, (C₅-C₁₀)heteroaryl-O-, (C₁-C₆)alkyl-(C=O)-O-, (C₃-C₁₀)cycloalkyl-(C=O)-O-, phenyl-(C=O)-O-, (C₅-C₁₀)heterocyclic-(C=O)-O-, (C₅-C₁₀)heteroaryl-(C=O)-O-, O₂N-, amino, (C₁-C₆)alkylamino, ((C₁-C₆)alkyl)₂-amino, formamidyl, (C₁-C₆)alkyl-(C=O)-NH-, (C₃-C₁₀)cycloalkyl-(C=O)-NH-, phenyl-(C=O)-NH-, (C₅-C₁₀)heterocyclic-(C=O)-NH-, (C₅-C₁₀)heteroaryl-(C=O)-NH-, (C₁-C₆)alkyl-(C=O)-[((C₁-C₆)alkyl)-N]-, phenyl-(C=O)-[((C₁-C₆)alkyl)-N]-, (C₁-C₆)alkyl-SO₂NH-, (C₃-C₁₀)cycloalkyl-SO₂NH-, phenyl-SO₂NH-, (C₅-C₁₀)heterocyclic-SO₂NH- and (C₅-C₁₀)heteroaryl-SO₂NH-;

wherein the phenyl or heteroaryl moiety of a R⁶ substituent is optionally further substituted with at least one radical independently selected from the group consisting of (C₁-C₆)alkoxy, perfluoro(C₁-C₆)alkyl and perfluoro(C₁-C₆)alkoxy.

15. (new) A compound according to claim 14 wherein R¹ can optionally be independently substituted with zero to two moieties independently selected from the group consisting of halo(C₁-C₆)alkyl, perhalo(C₁-C₆)alkyl, perhalo(C₁-C₆)alkoxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₅-C₁₀)ar(C₁-C₆)alkoxy, (C₅-C₁₀)heteroar(C₁-C₆)alkoxy, amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkylamino(C₁-C₆)alkyl, di(C₁-C₆)alkylamino(C₁-C₆)alkyl, and (C₅-C₁₀)heterocyclyl(C₁-C₆)alkyl.